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EXAMINER

STEELE, AMBER D

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Advisory Action Continued**

***Arguments and Response***

Applicants' arguments directed to the rejection under 35 USC 112, second paragraph (indefinite), for claim 10 were considered but are not persuasive for the following reasons.

Applicants contend that restriction enzymes are well-known in the art; base, modified base, and modification are defined in the specification; claim 15 was not part of the indefiniteness rejection; a nexus is present between the last method step and the preamble; and applicants request clarification regarding the additional errors.

Applicants' arguments are not convincing since (1) the term "restriction enzyme" was not considered indefinite in the rejection of record, but rather the language relating to the restriction enzyme (i.e. which can digest a DNA regardless of the presence or absence of a modification in a recognition site to generate a cohesive end containing a modified base or a base), (2) the definitions in the specification are noted, however, the definitions in the specification do not limit the terms from the art-recognized meanings (i.e. examples are provided, but the definition is not limited to the examples due to the language utilized in the definition) and the indefinite rejection is based on the language of the claim as a whole and not a specific term (i.e. unclear if a modification is actually required by the claimed method or not), (3) claim 15 was withdrawn and not examined in the previous Office action, (4) a nexus is not present because the preamble requires "analyzing a modification in a DNA to be assayed" while the last method step requires "analyzing all or part of DNA fragments contained in each of the DNA fragment groups with a DNA array" (i.e. analysis of a modification is not required), and (5) for clarity, the method of preparing the DNA fragments should be within method step (1) instead of after method step (3);

Art Unit: 1639

the comma between exposed and from is unnecessary (see step (1)); “in the step (1)” should be “in method step (1)”; commas within method step (2) are unnecessary; the claims are generally redundant in nature (i.e. claim limitations are actually not limiting in any way due to the alternative language in the claims regarding modified base or base); improper Markush language within method step (2); method step (3) should read “the DNA fragments”, (a) and (b) have unnecessary commas; (a) and (b) are not positive method steps for actually preparing the DNA fragments (e.g. is obtaining fragments required or actually the method of making the fragments?); etc.

Applicants’ arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Martinssen et al. and Makrigiorgos for claim 10 were considered but are not persuasive for the following reasons.

Applicants contend that Martinssen et al. does not teach restriction enzymes that digest gDNA in both the presence and absence of a modification of a base within the restriction enzyme recognition site wherein the modification is methylation and Makrigiorgos does not teach nuclease treatment before digesting the gDNA with the restriction enzyme or nuclease treatment of naturally occurring gDNA only.

Applicants’ arguments are not convincing since the teachings of Martinssen et al. and Makrigiorgos render the method of the instant claims *prima facie* obvious.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., restriction enzymes that digest DNA regardless of the methylation state, nuclease treatment is used to treat

Art Unit: 1639

naturally occurring gDNA only) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Martinssen et al. teach methods comprising utilizing various restriction enzymes (see the NEB information for methylation sensitivity of various restriction enzymes attached to the previous Office action) and “naturally occurring” gDNA (please refer to the entire specification particularly columns 1, 7, 9). Makrigiorgos teaches nuclease treatment (i.e. functions in the same manner regardless if present before or after ssDNA is present via restriction enzyme digestion; please refer to the entire specification particularly columns 7, 9, 11).

#### ***Future Communications***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1639

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/Amber D. Steele/  
Primary Examiner, Art Unit 1639